



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Heart, Lung, and
Blood Institute
Bethesda, Maryland 20892

December 19, 2019

Fernando Martinez, MD
PI, CleanUP-IPF Trial
Weill Cornell Medical College
525 East 68th Street, Room M-522
New York, NY 10065

Kevin Anstrom, PhD
PI, CleanUP-IPF Trial
Duke University School of Medicine
200 Morris Street
6320 200 Morris
Durham, NC 27701

Dear Drs. Martinez and Anstrom:

The purpose of this letter is to document formally the National Heart, Lung, and Blood Institute's (NHLBI) decision for early termination of the Study of Clinical Efficacy of Antimicrobial Therapy Strategy Using Pragmatic Design in Idiopathic Pulmonary Fibrosis (CleanUP-IPF) within the Pulmonary Trials Cooperative (PTC). This decision was informed by the recommendation of the Data and Safety Monitoring Board (DSMB) and subsequent NHLBI review as described below.

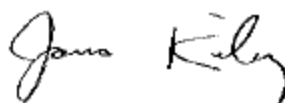
The DSMB met on December 18, 2019 to review the first planned efficacy analysis for CleanUp-IPF, and unanimously voted to terminate the study early for futility and to proceed with an orderly close-out. This determination was based on the low likelihood of the study demonstrating a statistically significant positive effect of the intervention. Although no clear harm signal was seen, the DSMB also noted a trend toward a higher rate of the primary outcome (non-elective respiratory hospitalization or all-cause mortality), mortality, and SAEs in the intervention arm, further supporting its recommendation to proceed to early orderly close-out. The DSMB recommends that the last study visit occur within 3 months (by mid-March) and patients may complete their course of study agent until their next (and last) visit.

The NHLBI carefully reviewed the DSMB recommendations. On December 19, 2019, Dr. Lora Reineck notified you of the intent of the Institute to concur with the DSMB recommendation for early termination.

The NHLBI is hopeful that we can achieve our shared goal of maximizing the information and generalizable knowledge gained from the study.

Thank you for your leadership on this important study.

Sincerely,

A handwritten signature in black ink that reads "James Kiley". The signature is written in a cursive style with a large initial "J" and "K".

James P. Kiley, Ph.D.
Director, Division of Lung Diseases
National Heart, Lung, and Blood Institute, NIH

cc:

Dr. Frank Scirba
Dr. Stephen Wisniewski
Dr. Tony Punturieri
Ms. Lisa Viviano
Mr. Andre Walker
Dr. Tom Croxton
Dr. Lora Reineck
Dr. Amy Patterson
Dr. Nakela Cook

Operations Memo CL023

TO: CleanUP IPF Clinical Site Principal Investigators and Lead Coordinators
FROM: NEMO and CleanUP IPF PLG
DATE: December 20, 2019
RE: End of Study Operations; Trial Card

CleanUP Operations Memos are posted on the PTC website under Documents – CleanUP Documents. Recipients are encouraged to download and file these memos for ready reference.

The purpose of this memo is to inform you that the CleanUP-IPF Data Safety Monitoring Board met on December 18, 2019 to review the first planned efficacy analysis for the trial, and unanimously voted to terminate the study early for futility and to proceed with an orderly study close-out. This determination was based on the low likelihood of the study demonstrating a statistically significant positive effect of the intervention. Although no clear harm signal was seen, the DSMB also noted a trend toward a higher rate of the primary outcome (non-elective respiratory hospitalization or all-cause mortality), mortality, and SAEs in the intervention arm, further supporting its recommendation to proceed to early orderly close-out.

The study PIs recommend contacting the individual patients on antimicrobial therapy to discontinue study treatment as soon as possible. All study patients, including those on standard of care, should be contacted by January 31 for a safety check and requested to have a final study visit scheduled and completed by March 13, 2020. Any visits scheduled prior to January 31 can be scheduled as end of study visits. A letter for the participants with more details will be sent in early January 2020.

Trial Card vouchers will be deactivated January 31, 2020.

A copy of the DSMB recommendation is included on pages two and three of this memo. ***This memo is not a close out letter.*** Your official close out letter will come on completion of all study visits and data queries.

Please submit this memo and the DSMB letter to your local IRB in the next two weeks. Once you have submitted to your IRB, please e-mail the NEMO at pulmonarytrials@edc.pitt.edu to let us know. You will also need to send a copy of your IRB's response letter to the same e-mail address

Please submit a Help Desk Ticket on the PTC website (<https://www.pulmonarytrials.org>) with any questions or concerns.